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EXAMINER

PAK, YONG D

ART UNIT PAPER NUMBER

1652

DATE MAILED: 02/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/089,175	Applicant(s) DALY ET AL.	
	Examiner Yong D. Pak	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 November 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,6,12,25-28 and 42-53 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,6,12,25-28 and 42-53 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This application is a continuation of PCT/US00/26504.

The amendment filed on November 23, 2005, amending claims 1-2, 12, 25 and 27-28, canceling claims 3-5, 7-11, 13-24 and 29-41 and adding claims 42-53, has been entered.

Claims 1-2, 6, 12, 25-28 and 42-53 are pending and are under consideration.

Response to Arguments

Applicant's amendment and arguments filed on November 23, 2005, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Objections

Claim 12 is objected to because of the following informalities: Claim 12 is objected for improper grammar. The claim recites the word "that" instead of "than" in line 2 which alters the overall meaning. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 6 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 depends from claim 41, which has been canceled, and therefore the limitations of said claim is highly unclear. Therefore, the claim has not been considered under other statutes.

Claims 1 and 52-53 and claims 2, 12, 25-28 and 42-51 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 52-53 recite the phrases "capable of detoxifying". A bacterium that "capable" of detoxifying a substance conveys that the bacterium detoxifies substances under some conditions but may have the same properties under all or other conditions. A bacterium "capable" of exhibiting a given activity may not have such property at all times or that such property is inherent to said bacterium. Therefore, it is not clear what are those conditions in which the bacterium is "capable of detoxifying" substances. Examiner requests clarification of the above phrase and suggests deleting said phrase. Furthermore, it is also unclear as to how the "*mer*" operon can detoxify a heavy metal. Perhaps it is the protein or other enzyme encoded by the "operon" that is responsible for detoxification. If that is so, Examiner suggests applicants to amend the claims accordingly.

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Claims 47 and 49-51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 47 and 49-51 recite the phrase "derivative thereof". The metes and bounds of this phrase in the context of the claims are not clear to the Examiner. Literally, the term "derivative" means a substance that can be made from another substance. Therefore, it is not clear to the Examiner either from the specification or from the claims as to what applicants mean by the above phrase. As applicants have not provided a definition for the above phrase, Examiner has interpreted the claims broadly to mean that a "derivative thereof" of "pMD66", "pMD727", "pMD728" and "pMD731" encompasses any variants or mutants of said plasmids.

Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 12 recites the phrase "at least one protein encode by a nucleic acid other than the *mer* operon". The metes and bounds of this phrase in the context of the claims are not clear to the Examiner. It is not clear to the Examiner either from the specification or from the claims as to what proteins are encompassed by the above phrase. Examiner requests clarification of the above phrase.

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The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 42 and 53 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 42 is drawn to a radiation resistant *Deinococcus* bacterium of claim 1, wherein said *Deinococcus* is *Deinococcus radiodurans* (strain ATCC BAA-816). However, *Deinococcus radiodurans* (strain ATCC BAA-816) was not described in the application as originally filed nor in any of its parent applications. Claim 53 is drawn to a radiation resistant, non-pathogenic bacterium. However, radiation resistant and non-pathogenic bacterium was not described in the application as originally filed nor in any of its parent applications. Therefore, claims 42 and 53 contain new matter.

Given this lack of description of *Deinococcus radiodurans* (strain ATCC BAA-816) and radiation resistant and non-pathogenic bacterium, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the inventions of claims 42 and 53 at the time of filing of the instant application.

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Claims 1-2, 12, 25-28 and 43-51 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-2, 12, 25-28 and 43-51 are drawn to a radiation resistant *Deinococcus* bacteria engineered to express heterologous proteins encoded by the *mer* operon and a bioremediation composition comprising said bacterium and a film forming or a nutrient agent, wherein the composition is formulated for controlled release. The claims encompass any or all *Deinococcus* bacteria transformed with any or all *mer* operon, including any or all mutants, derivatives, variants and recombinants thereof (claims 47 and 49-51), wherein said bacteria is able to detoxify any or all heavy metals. Therefore, these claims are drawn to a genus comprising any or all *Deinococcus* bacteria having any structure expressing a genus of *mer* operon having any structure, wherein the bacteria detoxifies any or all heavy metals. The specification only discloses a single species *D. radiodurans* transformed with a specific *mer* operon as described in Example 2, wherein the transformed bacterium detoxifies a single heavy metal, mercury. There is no evidence on the record of the relationship between the structure of a *D. radiodurans* expressing proteins encoded by the *mer* operon, wherein said bacteria detoxifies a single heavy metal, mercury, and the structure of any or all *Deinococcus* comprising any or all proteins encoded by a *mer* operon isolated from any source, including any or all variants, mutants, derivatives and recombinants thereof, wherein

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said bacteria detoxifies any or all heavy metals. Further, art teaches that *Deinococcus* bacterium, except *D. radiodurans* and *D. geothermalis*, are not transformable (Brim et al., page 4575). Therefore, the specification fails to describe a representative number of species comprising a genus of *Deinococcus* bacteria expressing any *mer* operon, wherein said bacteria are resistant to radiation and at the same time able to detoxify any heavy metals.

Given this lack of description of the representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the inventions of claims 1-2, 12, 25-28 and 43-51.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

In response to the previous Office Action, applicants have traversed the above rejection. Applicants should note that the rejection has been amended in light of the amendment of the claims.

Applicants argue that with the cancellation of claims 4 and 41 and amendment of claims 1, 2 and 6, the claims now encompass *Deinococcus* bacterium comprising a *mer* operon capable of detoxifying a heavy metal. Applicants argue the claims meet the written description requirement because the specification describes multiple species of *Deinococcus* bacterium containing a *mer* operon. Examiner respectfully disagrees. The claims are not limited to the specific *Deinococcus* disclosed on page 20, but the

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claims are drawn to a genus comprising any or all *Deinococcus* bacteria transformed with a genus comprising any or all *mer* operon, including any or all mutants, variants and recombinants thereof, wherein the resulting transformed bacteria detoxifies a genus comprising any or all heavy metals. The specification, however, only discloses a single species, *D. radiodurans* transformed with the *mer* operon described in Example 2, wherein the transformed bacterium detoxifies a single heavy metal, mercury. As discussed in the written description guidelines, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species which are adequately described are representative of the entire genus. **Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.** Satisfactory disclosure of a representative number depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species

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within the genus. In the instant case, the claims are drawn to a genus comprising any or all *Deinococcus* bacteria transformed with a genus comprising a *mer* operon having any structure, including any or all mutants, variants and recombinants thereof, wherein the resulting bacteria detoxifies a genus comprising any or all heavy metals. The genus of the claims are structurally diverse as it encompasses any or all *Deinococcus* bacteria transformed with any or all *mer* operon, wherein the resulting bacteria detoxifies any or all heavy metals. Further, art teaches that *Deinococcus* bacterium, except *D. radiodurans* and *D. geothermalis*, are not transformable (Brim et al., page 4575). As such, neither the description of solely functional features present in all members of the genus is sufficient to be representative of the attributes and features of the entire genus.

Claims 42 and 49-51 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The invention appears to employ novel plasmids and microorganism. Since the plasmids and microorganism are essential to the claimed invention, they must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The claimed plasmid's sequence is not fully disclosed, nor have all the sequences required for their construction been shown to be publicly known and freely available. The enablement requirements of 35 U.S.C. § 112 may be satisfied by a deposit

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of the plasmid. The specification does not disclose a repeatable process to obtain the plasmid and it is not apparent if the DNA sequences are readily available to the public.

It is noted that if applicants have deposited the plasmid, it must be public available. If the deposit was made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the specific strain has been deposited under the Budapest Treaty and that the strain will be available to the public under the conditions specified in 37 CFR 1.808, would satisfy the deposit requirement made herein.

If the deposit has not been made under the Budapest treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809, applicants may provide assurance or compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that: 1. during the pendency of this application, access to the invention will be afforded to the Commissioner upon request; 2. upon granting of the patent the strain will be available to the public under the conditions specified in 37 CFR 1.808; 3. the deposit will be maintained in a public repository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer; and 4. the deposit will be replaced if it should ever become inviable.

Claims 1-2, 12, 25-28 and 43-51 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a radiation resistant *D. radiodurans* transformed to specifically express the mercuric reductase encoded by the

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mer operon (as in Example 2) that confers mercury resistance function to *E. coli*, such that the transformed bacteria is radiation resistant (ionizing radiation) and detoxifies mercury, does not reasonably provide enablement for any or all *Deinococcus*, transformed to any or all *mer* operon from any source, wherein the transformed bacteria detoxifies any or all heavy metals. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Claims 1-2, 12, 25-28 and 42-53 are drawn to a radiation resistant *Deinococcus* bacteria engineered to express heterologous proteins encoded by the *mer* operon and a bioremediation composition comprising said bacterium and a film forming or a nutrient agent, wherein the composition is formulated for controlled release. The claims encompass any or all *Deinococcus* bacteria transformed with any or all *mer* operon, including any or all mutants, variants and recombinants thereof, wherein said bacteria is able to detoxify any or all heavy metals. Therefore, these claims are drawn to any or all

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Deinococcus bacteria having any structure expressing any or all mer operon having any structure, wherein the bacteria detoxifies any or all heavy metals.

The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of *Deinococcus* bacterium engineered with any or all mer operon to detoxify any or all heavy metals. Since each *Deinococcus* species behaves differently, predictability of which modifications can be tolerated by any or all *Deinococcus* that results in a radiation resistant bacteria that detoxifies heavy metals requires a knowledge and guidance with regard to which *Deinococcus* bacteria and mer operon to use and how tolerant the bacteria and proteins encoded by the mer operon are to such modifications such that the modified bacterium continues to have said claimed activity. While microbiological techniques, recombinant and mutagenesis techniques are known, and it is routine in the art to screen for multiple species or multiple modifications as encompassed by the instant claims, the specific *Deinococcus* species in which modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given bacteria to diminish with each further and additional modification. Further, art teaches that *Deinococcus* bacterium, except *D. radiodurans* and *D. geothermalis*, are not transformable (Brim et al., page 4575). Also, while enzyme isolation techniques, recombinant and mutagenesis techniques are known, and it is routine in the art to screen for multiple substitutions or multiple modifications as encompassed by the instant claims, the specific amino acid positions within a protein's

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sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

Therefore, it would require undue experimentation of the skilled artisan to make any *Deinococcus* expressing proteins encoded by any or all *mer* operon from any source, wherein said bacteria detoxifies any heavy metals. The specification is limited to the teaching of a *D. radiodurans* transformed with the *mer* operon (as in Example 2), wherein the transformed bacterium detoxifies a single heavy metal, mercury. In view of the great breadth of the claims, amount of experimentation required to make the claimed bacterium, the lack of guidance, working examples, and unpredictability of the art in predicting which techniques to engineer any *Deinococcus* bacterium to detoxify any heavy metal or which *mer* operon to use to transform said bacteria, the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the method encompassed by the claims.

The specification does not support the broad scope of the claims which encompass any or all *Deinococcus* bacterium, including any or all mutants, variants, and recombinants transformed to express proteins encoded by any or all *mer* operon from any source, wherein said bacteria detoxifies any or all heavy metals because the specification does not establish: (A) *Deinococcus* bacteria which may be modified

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without that results in a radiation resistant bacteria that also detoxifies heavy metals; (B) microbiological techniques which may be used to modify any or all *Deinococcus* bacteria that results in a in a radiation resistant bacteria that also detoxifies heavy metals; (C) a rational and predictable scheme for modifying any *Deinococcus* bacteria using any techniques with an expectation of obtaining the desired biological function; (D) the general tolerance of any or all *Deinococcus* bacterium to modification by any or all techniques and extent of such tolerance; regions of the protein structure which may be modified without affecting cytokinin oxidase activity; (E) the general tolerance of proteins encoded by the mer operon to modification and extent of such tolerance; (F) a rational and predictable scheme for modifying any amino acid residue with an expectation of obtaining the desired biological function; and (G) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any or all *Deinococcus* bacterium, including any or all mutants, variants, and recombinants engineered to express proteins encoded by any *mer* operon from any source, wherein the transformed bacteria detoxifies any or all heavy metals. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of which *Deinococcus* bacteria to modify and which mer operon to use is unpredictable and the experimentation left to those skilled in

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the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In response to the previous Office Action, applicants have traversed the above rejection. Applicants should note that the rejection has been amended in light of the amendment of the claims.

Applicants argue that the "Examiner purports that the specification, while enabling for a radiation resistant *D. radiodurans* transformed to express proteins encoded by the *mer* operon, does not reasonable provide enablement for any or all bacterium". Examiner respectfully disagrees. The rejection stated:

"while being enabling for a radiation resistant *D. radiodurans* transformed to express proteins encoded by the *mer* operon isolated from *E.coli*, such that the transformed bacteria is radiation resistant (ionizing radiation) and detoxifies mercury, does not reasonably provide enablement for any or all bacterium, including any or all mutants, variants, and recombinants engineered to express proteins encoded by a *mer* operon from any source, or engineered by any or all types of techniques to detoxify any or all toxins, radionuclides, heavy metals or organic compound."

Applicants also argue that the same claims have been rejected for both being obvious and lacking enablement (claims 1 to 4, 6 and 12), and that it is unclear to applicants how the skilled artisan would find such claims lacking enablement if it would be obvious to the skilled artisan to reproduce the claims without undue experimentation. Examiner respectfully disagrees with such an argument. The enablement rejection now argues that applicants are indeed enabled for the *D. radiodurans* transformed with the specific *mer* operon as in Example 2, but not enabled for such a bacterium transformed with any or all *mer* operon. Examiner has also shown that what is enabled is also

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obvious in the rejection under 35 USC 103(a). However, Examiner has not argued that it would be obvious to transform *D. radiodurans* using any *mer* operon and obtain a bacterium capable of detoxifying mercury. Therefore, contrary to applicants' argument, Examiner has not imposed an improper enablement and obviousness rejection.

Applicants also argue that claims meet the enablement requirement because the claims now encompass *Deinococcus* bacterium comprising a *mer* operon capable of detoxifying a heavy metal and cites Brim et al. (2003) to support that *Deinococcus* bacterium are naturally transformable and the skilled artisan could readily transform the *mer* operon into any strain of *Deinococcus* without undue experimentation. Examiner respectfully disagrees. Examiner found no such support in Brim et al. Contrary to applicants arguments, Brim et al. teaches the opposite of what applicants are arguing. Brim et al. actually teaches that *Deinococcus* bacterium, except *D. radiodurans* and *D. geothermalis*, are not transformable. The relevant passage of Brim et al. is reiterated here for applicant's convenience.

strain R1 is the best characterized (4). Advances in genetic engineering for *D. radiodurans* (9–12, 29) were a stimulus for its genome sequencing (17, 33), annotation (22), and proteomic (18) and transcriptome (19) analyses. The other deinococcal species have been reported as nontransformable or have not yet been tested for transformability by chromosomal or plasmid DNA and have been left unexplored by recombinant DNA technologies. Other genetic approaches including conjugation and protoplast fusion have not been successful in the *Deinococcaceae* (16).

A unique genetic engineering goal for *D. radiodurans* is its

Further, the claims are not limited to the specific *Deinococcus*, such as *D. radiodurans*, but the claims are drawn to any or all *Deinococcus* bacteria transformed with any or all *mer* operon, including any or all mutants, variants and recombinants thereof, wherein

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the resulting bacteria detoxifies any or all heavy metals. The specification, however, only teaches a single species *D. radiodurans* transformed with the *mer* operon, wherein the transformed bacterium detoxifies a single heavy metal, mercury. As discussed above, predictability of which modifications can be tolerated by any or all *Deinococcus* and *mer* operon that results in a radiation resistant bacteria that detoxifies heavy metals requires a knowledge and guidance with regard to which *Deinococcus* bacteria and *mer* operon to use and how tolerant the bacteria and proteins encoded by the *mer* operon are to such modifications such that the modified bacterium continues to have said claimed activity. It is this specific guidance that applicants do not provide. Without specific guidance, those skilled in the art will be subjected to undue experimentation of making and testing each of the enormously large number of mutants that results from such experimentation.

Hence the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

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the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2, 12, 25-28 and 42-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hamlett et al. and Daly et al.

Claims 1-2, 12, 25-28 and 42-53 are drawn to radiation resistant *D. radiodurans* engineered to express proteins encoded by a *mer* operon, wherein the bacterium grows in the presence of continuous radiation of about 60 Gy/hour and in the presence of 100 μ M mercury, detoxifies heavy metals and wherein the *mer* operon is constitutively expressed and expressed from an autonomously replicating plasmid or derivatives of plasmids pMD66, pMD727, pMD728 and pMD731 (see rejection of the phrase "derivative thereof" under 35 USC 112, 2nd paragraph).

Hamlett et al. (form PTO-1449) discloses a plasmid comprising a *mer* operon that encodes six proteins that confer mercury resistance functions on *E. coli* (pages 6377 and 6382-6383), the same *mer* operon used by applicants (Example 2). Hamlett et al. teaches that the transformed bacterium converts toxic mercury (Hg^{2+}) to the less toxic elemental form, Hg^0 , is resistant to 100 μ M mercury (pages 6381).

The difference between the reference of Hamlett et al. and the instant invention is that Hamlett et al. does not teach a radiation resistant *D. radiodurans* expressing proteins encoded by a *mer* operon, wherein the *mer* operon is expressed constitutively by an autoreplicating plasmid.

Daly et al. (form PTO-892) discloses that radiation resistant *D. radiodurans* is naturally transformable and is amenable to genetic manipulation (pages 3508 and 3509). Daly et al. teaches how to express heterologous proteins in *D. radiodurans* using an autoreplicating plasmid pMD66 (page 3509), which is the same plasmid used by applicants (specification page 37). Daly et al. also teaches that said *D. radiodurans* is able to grow in the presence of continuous ionizing radiation exposure (page 3510). One having ordinary skill in the art would have recognized the advantage of making a bacterium having resistance to both radiation and mercury, for its application in detoxifying mercury contaminated radioactive wastes. Also since "derivative thereof" of "pMD66" has been interpreted to broadly encompasses any variants or mutants of said plasmids, the plasmid of Daly et al. encompasses derivatives of "pMD66" "pMD727", "pMD728" and "pMD731".

Therefore, combining the teachings of the above two references, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to engineer a *D. radiodurans* of Daly et al. to express proteins encoded by a *mer* operon taught by Hamlett et al, wherein the *mer* operon is expressed constitutively via an auto replicating plasmid. One of ordinary skill in the art would have been motivated to make a bacterium having resistance to both radiation and mercury, for its application

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in detoxifying mercury contaminated radioactive wastes and make a biological deposit of the bacterium. One of ordinary skill in the art would have had a reasonable expectation of success in expressing proteins encoded by the *mer* operon in *D. radiodurans* since Hamlett et al. teaches plasmids comprising said operon and Daly et al. teaches how to transform *D. radiodurans* with foreign polynucleotides using an autoreplication plasmid.

Therefore, Hamlett et al. and Daly et al. render claims 1-4, 6, 12, 25 and 41 *prima facie* obvious to those skilled in the art.

In response to the previous Office Action, applicants have traversed the above rejection. Applicants should note that the rejection has been amended in light of the amendment of the claims.

Applicants also argue use of improper hindsight reasoning. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In the instant case, it should be noted that the knowledge of transforming *D. radiodurans* with said genes was well known and within the level of one having ordinary skill in the art at the time the invention was made.

Applicants also argue that Carroll et al. does not disclose the growth of *Deinococcus* in the presence of continuous ionizing radiation. Carroll et al. has been removed from the rejection. However, Daly et al. teaches that *D. radiodurans* transformed with the *mer* operon is able to grow in the presence of continuous ionizing radiation exposure (page 3510). Also, the ability of transformed *D. radiodurans* to grow in continuous ionizing radiation is an inherent property of said bacteria. The property is expected since wild type *D. radiodurans* is extremely resistant to ionizing radiation (Daly et al. page 3508).

Applicants also argues that Carroll et al. discloses expression of a heterologous protein using an inducible promoter, whereas the claims now are drawn to expression of a constitutively active *mer* operon. Carroll et al. has been removed from the rejection. However, Daly et al. teaches how to express heterologous proteins in *D. radiodurans* using an autoreplicating plasmid pMD66 (page 3509), which is the same plasmid used by applicants (specification page 37).

Hence the rejection is maintained.

Claims 25-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hamlett et al. and Daly et al. as applied to claims 1-2, 12, 25-28 and 42-53 above, and further in view of Lin et al.

Claims 25-28 are drawn to a bioremediation composition comprising a radiation resistant *D. radiodurans* engineered to detoxify heavy metals, film forming agents and a nutrient agent, wherein the composition is formulated for controlled release.

Hamlett et al and Daly et al. in combination teach a radiation resistant *D. radiodurans* engineered to detoxify heavy metals, as discussed above.

The difference between the combined references of Hamlett et al. and Daly et al. and the instant invention is that a bioremediation composition comprising a radiation resistant *D. radiodurans* engineered to detoxify heavy metals is not taught.

Lin et al. (WO 95/08513 – form PTO-892) discloses a bioremediation composition comprising bacteria, film forming agents and nutrient agents, wherein the composition is formulated for controlled release (abstract and pages 1-2). Lin et al. teaches that said composition formulated for controlled release with film forming agents and nutrient agents enhances biodegradation of toxic compounds (page 5).

Therefore, combining the teachings of the above three references, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to formulate a *D. radiodurans* transformed with a *mer* operon for controlled release by using film forming agents and nutrient agent. One of ordinary skill in the art would have been motivated to make such a composition in order to enhance biodegradation of mercury contaminated radioactive wastes. One of ordinary skill in the art would have had a reasonable expectation of success in making such a composition since Lin et al. teaches how to formulate bioremediation compositions comprising bacteria for controlled release using film forming agents and nutrient agents and Hamlett et al. and Daly et al. in combination teaches a radiation resistant *D. radiodurans* that detoxifies mercury.

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Therefore, Hamlett et al., Daly et al. and Lin et al. render claims 25-28 *prima facie* obvious to those skilled in the art.

In response to the previous Office Action, applicants have traversed the above rejection. Applicants argue that for the reasons discussed above rejection, applicants submit that skilled artisan would not be motivated to apply Carrol et al. to the claimed invention.

Applicants should note that the rejection has been amended in light of the amendment of the claims. The rejection now cites Daly et al., the teachings of which have been discussed above. Therefore, combining the teachings of the above three references, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to formulate a *D. radiodurans* transformed with a *mer* operon for controlled release by using film forming agents and nutrient agent.

Hence the rejection is maintained.

None of the claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within

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TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Yong D. Pak
Patent Examiner



Manjunath Rao

Primary Patent Examiner 1652